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COMMENTARY - NEUROSURGERY

In this issue we have selected three recently published research papers from prominent Neurosurgery journals. The first is an interesting paper looking to further explore the pathophysiology behind idiopathic normal pressure hydrocephalus, by comparing corticospinal excitability of NPH patients before and after a definitive diversion procedure, as well as comparing it to normal subjects. The second is a paper which prospectively randomizes patients with aneurysmal subarachnoid hemorrhage and traumatic brain injury, to study the relative effectiveness of either the modified Lund concept or cerebral perfusion pressure-targeted therapy (CPP-targeted) for their management. The third paper is a supplemental analysis of the 5-aminolevulinic acid (ALA) glioma study and questions the role of extended resections by looking into new onset neurological impairments.

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MOTOR CORTEX DISINHIBITION IN NORMAL-PRESSURE HYDROCEPHALUS

OBJECT: Previous studies have shown a close association between frontal lobe dysfunction and gait disturbance in idiopathic normal-pressure hydrocephalus (iNPH). A possible mechanism linking these impairments could be a modulation of corticospinal excitability. The aim of this study was 2-fold: 1) to determine whether iNPH affects corticospinal excitability; and 2) to evaluate changes in corticospinal excitability following ventricular shunt placement in relation to clinical outcome.

METHODS: Twenty-three patients with iNPH were examined using single- and paired-pulse transcranial magnetic stimulation of the leg motor area before and 1 month after ventricular shunt surgery. The parameters of corticospinal excitability assessed were the resting motor threshold (rMT), motor evoked potential/M-wave area ratio, central motor conduction time, intracortical facilitation, and short intracortical inhibition (SICI). The results were compared with

those obtained in 8 age-matched, healthy volunteers, 19 younger healthy volunteers, and 9 age-matched patients with peripheral neuropathy.

RESULTS: Significant reduction of the SICI associated with a decrease of the rMT was observed in patients with iNPH at baseline evaluation. Ventricular shunt placement resulted in significant enhancement of the SICI and increase of the rMT in patients who markedly improved, but not in those who failed to improve.

CONCLUSIONS: This study demonstrates that iNPH affects corticospinal excitability, causing disinhibition of the motor cortex. Recovery of corticospinal excitability following ventricular shunt placement is correlated with clinical improvement. These findings support the view that reduced control of motor output, rather than impairment of central motor conduction, is responsible for gait disturbances in patients with iNPH.

Clin Neurol Neurosurg. 2011 Oct 28. [Epub ahead of print]

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MODIFIED LUND CONCEPT VERSUS CEREBRAL PERFUSION PRESSURE-TARGETED THERAPY: A RANDOMISED CONTROLLED STUDY IN PATIENTS WITH SECONDARY BRAIN ISCHAEMIA

PURPOSE: Secondary brain ischaemia (SBI) usually develops after aneurysmal subarachnoid haemorrhage (SAH) and severe traumatic brain injury (TBI). Current approaches to managing these conditions are based either on intracranial pressure-targeted therapy (ICP-targeted) with cerebral microdialysis (CM) monitoring according to the modified Lund concept or cerebral perfusion pressure-targeted

therapy (CPP-targeted). We present a prospective, randomised controlled study comparing relative effectiveness of the two management strategies.

METHODS: Sixty comatose operated patients with SBI following aneurysmal SAH and severe TBI were randomised into ICP-targeted therapy with CM monitoring and CPP-targeted therapy groups. Mortality rates in both groups were calculated and tissue biochemi-

biochemical signs of cerebral ischaemia were analysed using CM. Measured CM data were related to outcome (Glasgow Outcome Scale [GOS] score 1, 2 and 3 for poor outcome or GOS score 4 and 5 for good outcome). **RESULTS:** Patients treated with ICP-targeted therapy with CM monitoring had significantly lower mortality rate as compared with those treated with CPP-targeted therapy ($P=0.03$). Patients monitored with CM who had poor outcome had lower mean values of glucose and higher mean values of glycerol and lactate/pyruvate ratio as compared with those who had good outcome (glucose: $P=0.003$; glycerol: $P=0.02$; lactate/pyruvate ratio: $P=0.01$).

There was no difference in the mortality outcome between aneurysmal SAH and severe TBI in the two groups ($P=0.28$ for ICP-targeted therapy with CM monitoring, $P=0.36$ for CPP-targeted therapy). Also, there were no differences in the CM values between patients with aneurysmal SAH and severe TBI who underwent ICP-targeted therapy (glucose: $P=0.23$; glycerol: $P=0.41$; lactate/pyruvate ratio: $P=0.40$). **CONCLUSION:** The modified Lund concept, directed at bedside real-time monitoring of brain biochemistry by CM showed better results compared to CPP-targeted therapy in the treatment of comatose patients sustaining SBI after aneurysmal SAH and severe TBI.

J Neurosurg. 2011 Mar;114(3):613-23. Epub 2010 Apr 16.

Stummer W, Tonn JC, Mehdorn HM, Nestler U, Franz K, Goetz C, Bink A, Pichlmeier U; ALA-Glioma Study Group. Collaborators (38)

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COUNTERBALANCING RISKS AND GAINS FROM EXTENDED RESECTIONS IN MALIGNANT GLIOMA SURGERY: A SUPPLEMENTAL ANALYSIS FROM THE RANDOMIZED 5-AMINOLEVULINIC ACID GLIOMA RESECTION STUDY. CLINICAL ARTICLE

OBJECT: Accumulating data suggest more aggressive surgery in patients with malignant glioma to improve outcome. However, extended surgery may increase morbidity. The randomized Phase III 5-aminolevulinic acid (ALA) study investigated 5-ALA-induced fluorescence as a tool for improving resections. An interim analysis demonstrated more frequent complete resections with longer progression-free survival (PFS). However, marginal differences were found regarding neurological deterioration and the frequency of additional therapies. Presently, the authors focus on the latter aspects in the final study population, and attempt to determine how safety might be affected by cytofluorescence-guided surgery. **METHODS:** Patients with malignant gliomas were randomized for fluorescence-guided (ALA group) or conventional white light (WL) (WL group) microsurgery. The final intent-to-treat population consisted of 176 patients in the ALA and 173 in the WL group. Primary efficacy variables were contrast-enhancing tumor on early MR imaging and

6-month PFS. Among secondary outcome measures, the National Institutes of Health Stroke Scale (NIH-SS) score and the Karnofsky Performance Scale (KPS) score were used for assessing neurological function. **RESULTS:** More frequent complete resections and improved PFS were confirmed, with higher median residual tumor volumes in the WL group (0.5 vs 0 cm³, $p = 0.001$). Patients in the ALA group had more frequent deterioration on the NIH-SS at 48 hours. Patients at risk were those with deficits unresponsive to steroids. No differences were found in the KPS score. Regarding outcome, a combined end point of risks and neurological deficits was attempted, which demonstrated results in patients in the ALA group to be superior to those in participants in the WL group. Interestingly, the cumulative incidence of repeat surgery was significantly reduced in ALA patients. When stratified by completeness of resection, patients with incomplete resections were quicker to deteriorate neurologically ($p = 0.0036$).

CONCLUSIONS: Extended resections performed using a tool such as 5-ALA-derived tumor fluorescence, carries the risk of temporary impairment of neurological function. However, risks are higher in patients with deficits unresponsive to steroids.